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**Macromolecular Control of Structural Organization  
in Thin Molecular Films:  
Implications for Chemical and Optical Switching**

**FINAL REPORT**

**David A. Tirrell**

**September 1, 1991**

**U.S. Army Research Office  
Grant No. DAAL03-88-K-0038**

**University of Massachusetts**

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## **Statement of the Problem**

The objectives of this program concerned the development of new ultrathin membranes that respond to well-defined chemical and physical signals. Such membranes are proposed to be useful in applications such as chemical sensing and controlled chemical delivery.

The mechanism by which these membranes respond to signals involves changes in the conformation and solvation of surface-bound polyelectrolyte chains. Because polyelectrolytes can be rendered sensitive to many different environmental parameters (e.g., pH, light, ionic strength, etc.) this approach provides a new route to molecular films subject to switching in response to many different (and useful) stimuli. To date, we have prepared membrane systems switchable with pH, temperature, light, glucose concentration, ionic strength, and electrochemical reduction.

## **Summary of Results**

**Molecular Weight Dependence of Polyelectrolyte Activity.** We have found that samples of poly(2-ethylacrylic acid) (PEAA) behave in similar fashion as membrane switching agents, as long as the weight-average molecular weight ( $\bar{M}_w$ ) is greater than ca. 40,000. At ( $\bar{M}_w$ )=12,000, the cooperativity of both the conformational transition of PEAA and the PEAA-driven vesicle-to-micelle transition of dipalmitoylphosphatidylcholine (DPPC) was reduced, and each transition was shifted to lower pH. A manuscript describing these results has been published in *Macromolecules* (22, 765, 1989).

**Kinetics of Membrane Reorganization.** We have completed a light-scattering study of the PEAA-driven reorganization of membranes formed from dioleoylphosphatidylcholine (DOPC). The kinetics of membrane reorganization, and the time-course of the evolution of the particle size distribution, have been determined. Electrophoretic light scattering reveals an increase in surface charge density at low pH as a result of polyelectrolyte adsorption. A

manuscript describing these results has been published in *Macromolecules* (22, 2755, 1989).

**Light-sensitive Vesicle Membranes.** Light-sensitive systems of two kinds were developed. First, polyelectrolytes bearing spirobenzopyran functions were prepared and shown to exhibit photoregulated binding to phosphatidylcholine membranes. These systems are complementary to our previously reported azobenzene-modified polymers, in that irradiation causes an *increase* in membrane permeability rather than a decrease, as was previously observed. In each case, the permeability change can be rationalized on the basis of differences in the solvation of the chromophores in their dark-adapted and irradiated states. The second approach to photosensitization exploits 3,3'-dicarboxyphenyliodonium (DCPI) salts to generate protons in response to light. Irradiation of DCPI salts in suspensions of phosphatidylcholines causes a depression of pH; in the presence of poly(2-ethylacrylic acid) (PEAA), polyelectrolyte-induced membrane reorganization and loss of barrier properties result. These experiments were reported in the *Journal of the American Chemical Society* (113, 4022, 1991).

**Electrochemical Switching.** Electrochemical switching has been accomplished via reduction of ferrocenyl functions bound in small numbers to low molecular weight poly(methacrylic acid)s. Release of vesicle-entrapped solutes can be accomplished in pulsatile fashion through controlled reduction of these polymers in phosphatidylcholine suspensions.

**Compositional Control of Membrane Switching Properties.** We have determined reactivity ratios for the radical copolymerization of methacrylic acid and 2-ethylacrylic acid. This copolymerization is highly medium-dependent, and provides a range of copolymers that effect membrane switching at any pH between ca. 5.8 and 6.8. The copolymerization study has been published in the *Journal of Polymer Science* (28, 3155, 1990).

**Solution Behavior of Poly(*N*-isopropylacrylamide) (PNIPAAm).** The objective of this portion of our work has been the exploitation of the lower critical solution temperature (LCST) of PNIPAAm to effect membrane reorganization in response to thermal signals. This has prompted a detailed calorimetric investigation of the LCST of PNIPAAm and several other polymers in aqueous solution (*Journal of Phys. Chem.* **94**, 4352, 1990) as well as the development of sodium 2-(*N*-dodecylamino)naphthalene-6-sulfonate as a fluorescence probe of polymer-surfactant interaction *Langmuir* (**6**, 1676, 1990).

**Interaction of PNIPAAm with Surfactants.** We have completed a careful study of the interaction of PNIPAAm with sodium *n*-alkyl sulfates in aqueous solution. In general, PNIPAAm promotes surfactant aggregation, and enjoys enhanced water solubility (as reflected in elevation of the LCST) as a result of the binding of surfactant micelles. Both these effects become most apparent as the length of the surfactant tail increases, and are lost at chain lengths of 4 or less. At surfactant concentrations less than those required for micellar binding, the LCST of PNIPAAm is depressed with respect to the LCST of the polymer in pure water. Surfactant aggregation is reported by the fluorescent probes pyrene, 1-pyrenecarboxaldehyde, and sodium 2-(*N*-dodecylamino)naphthalene-6-sulfonate, but not by 1-benzoylacetone. The emission behavior of the pyrene and naphthalene probes suggests that polymer-bound micelles are somewhat less polar than the corresponding surfactant aggregates formed in polymer-free solution. The theory of Nagarajan and Ruckenstein, in a form that assigns the polymer the role of modulating the tension at the micelle-water interface, is successful in predicting the observed aggregation behavior of all but the shortest chain length surfactants. This work has been published in *Langmuir* (**7**, 665, 1991).

**Polypeptides as Membrane Switches.** The potential advantages of polypeptides in this role are: first, their biocompatibility; and second, the precision with which polypeptide structure and function can be engineered through the use of recombinant DNA methods. In our initial experiments in this area, we prepared statistical copolymers of valine and glutamic acid, in

the hope that the hydrophobic valine residues would confer on the copolymer a globular structure at low pH. The globular polymer was expected to bind to the bilayer membrane and thereby to effect useful changes in membrane permeability. In fact, the copolymers themselves did not behave in this fashion, but required further modification via attachment of a small number of C6-C8 alkyl chains. The modified polypeptides then worked well as membrane switches.

We have also accomplished the expression of an artificial gene that encodes a cleavable fusion protein with a poly(glutamic acid) fragment of molecular weight 10,000. The fusion protein has been isolated and purified, and the poly(glutamic acid) fragment liberated. This development provides a route to monodisperse samples of poly(glutamic acid) and its derivatives, which can be used as well-defined, biodegradable membrane switches.

## PUBLICATIONS

H.G. Schild and D.A. Tirrell, "Microcalorimetric Detection of Lower Critical Solution Temperatures in Aqueous Polymer Solutions," *Journal of Physical Chemistry*, 94, 4352, 1990.

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M. Maeda, A. Kumano and D.A. Tirrell, "Signal-Sensitive Release of Contents from Liposomes Bearing Surface-Grafted Polyelectrolyte Chains," *Annals of New York Academy of Sciences*, 618, 362, 1991.

H.G. Schild, "Probes of the Lower Critical Solution Temperature of Poly(N-isopropylacrylamide)," *ACS Symposium Series*, in press.

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H. You and D.A. Tirrell, "Radical Copolymerization of 2-Ethylacrylic Acid and Methacrylic Acid," *Journal of Polymer Science Part A: Polymer Chemistry*, 28, 3155, 1990.

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K.M. Eum, K.H. Langley and D.A. Tirrell, "Quasi-Elastic and Electrophoretic Light Scattering Studies of the Reorganization of Dioleoylphosphatidylcholine Vesicle Membranes by Poly(2-ethylacrylic acid)," *Macromolecules*, 22, 2755, 1989.

## Technical Reports

Technical reports were submitted to ARO as requested for the following periods:

July 1, 1988 - December 31, 1988  
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January 1, 1991 - June 30, 1991

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Michael S. Ferritto, Ph.D. awarded  
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